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JC14 Rec'd PCT/PTO 14 JAN 2002

Form PTO-1390 (Rev. 12-29-99) US DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NO.
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371	**H 4172 PCT/US**
	U.S. APPLICATION NO. (if known see 37 CFR 1.5) 10/030974

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP00/06162	**July 1, 2000**	**July 12, 1999**

TITLE OF INVENTION
PREPARATIONS CONTAINING NO CROSS-LINKING AGENTS

APPLICANT(S) FOR DO/EO/US
Andrea Heilemann, Josef Holzer, Andreas Sander, Gisbert Schaefer

Applicant herewith submits to the United States Designated/Elected Office (EO/DO/US) the following items and other information:

1. ■ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. □ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. □ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39 (1).
4. ■ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ■ A copy of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. □ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ■ has been transmitted by the International Bureau.
   c. □ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ■ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ■ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. □ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. □ have been transmitted by the International Bureau.
   c. □ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ■ have not been made and will not be made.
8. □ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ■ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). **(UNEXECUTED)**
10. □ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. □ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. □ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ■ A FIRST preliminary amendment
    □ A SECOND or SUBSEQUENT preliminary amendment.
14. □ A substitute specification.
15. □ A change of power of attorney and/or address letter.
16. □ Other items or information:

"Express Mail Post Office to Addressee" service Mailing Label Number EL541613885US .

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JC13 Rec'd PCT/PTO 14 JAN 2002

U.S. Application No. (If known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
10/030974	PCT/EP00/06162	H 4172 PCT/US

17.■ The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)):

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO.....**$1,040.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO.....**$890.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37CFR 1.445(a)(2)) paid to USPTO **$740.00**

International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$710.00**

International preliminary examination fee paid to USPTO (37CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4).....**$100.00**

	CALCULATIONS	PTO USE ONLY
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date 37 (CFR 1.492(e)).	$ 0	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	20 - 20 =	0	0 X $18.00	$ 0	
Independent Claims	2 - 3 =	0	0 X $84.00	$ 0	
Multiple dependent claims (s)(if applicable)		0	+ $280.00	$ 0	
TOTAL OF ABOVE CALCULATIONS =				$ 890	
Reduction of ½ for filing by small entity, if applicable. A Small Entity Statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$ 0	
SUBTOTAL =				$ 890	
Processing fee of **$130.00** for furnishing the English translation later the ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				$ 0	
TOTAL NATIONAL FEE =				$ 890	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property +				$ 0	
TOTAL FEES ENCLOSED =				$ 890	
				Amount to be: refunded:	$----------
				charged:	$890.00

a. ☐ A check in the amount of $_____ to cover the above fees is enclosed.

b. ■ Please charge my Deposit Account No. 50-1177 in the amount of $890.00 to cover the above fees. A triplicate copy of this sheet is enclosed. Order No. 02-0014.

c. ■ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-1177. A triplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
Cognis Corporation, Law Dept.
2500 Renaissance Blvd., Suite 200
Gulph Mills, PA 19406

John E Drach
SIGNATURE:

John E. Drach
NAME ATTORNEY FOR APPLICANT

32,891
REGISTRATION NUMBER

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"Express Mail " Mailing Label Number EL541613885US .

PATENT
Docket No. H 4172 PCT/US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RE: PCT/EP00/06162
International Filing Date: July 1, 2000
Priority Date Claimed: July 12, 1999
Applicant: Heilemann, et al.
Title: PREPARATIONS CONTAINING NO CROSS-LINKING AGENTS
Applicants' Reference: H 4172 PCT/US

PRELIMINARY AMENDMENT

Commissioner for Patents
Box PCT
Washington, DC 20231

ATTN: DO/EO/US

Prior to the calculation of fees and examination of the above-identified national stage application pursuant to the accompanying submission under 35 U.S.C. §371, please amend the English translation of the International Application submitted herewith, without prejudice, as follows:

In the Specification:

Please amend the instant Specification, without prejudice, as follows:

Please delete all text above line 7 of page 1, including the heading "Prior Art", and replace the deleted matter with the following new section headings and title of the invention:

--TITLE OF THE INVENTION

Processes for Preparing Crosslinker-Free, Biopolymer-Containing Three Dimensional Structures, and Products Prepared Thereby

BACKGROUND OF THE INVENTION--

At page 3, line 3 thereof, please delete the section heading "Description of the

Invention" and the entire paragraph spanning lines 4 through 6 of page 3, and insert the following new section heading and new paragraphs:

--BRIEF SUMMARY OF THE INVENTION

The present invention relates, in general, to biopolymers and crosslinker-free preparations obtained by precipitation and subsequent drying of chitosans, and to a process for their production.

Thus, the present invention includes a crosslinker-free preparation obtainable by adding a precipitant to an aqueous solution and/or homogenized suspension of a chitosan and then drying.--

At page 4, line 15 thereof, please insert the following new section heading:

--DETAILED DESCRIPTION OF THE INVENTION--

At page 27, between lines 1 and 2, please add the following new paragraph:

--What is claimed is:--.

On a separate, new page 29, please add the following new section heading and paragraph containing an Abstract of the Disclosure:

--ABSTRACT OF THE DISCLOSURE

Processes for preparing crosslinker-free, chitosan-containing compositions, comprising: (a) providing an aqueous mixture of a chitosan, wherein the aqueous mixture has a viscosity of from 1,000 mPas to 100,000 mPas; (b) combining a precipitant with the aqueous mixture to form a crosslinker-free chitosan composition; and (c) drying the crosslinker-free chitosan composition to form a crosslinker-free three-dimensional structure; are described. Also described are three-dimensional structures prepared thereby and uses therefor in cosmetics, food additives and medical products.--

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In the Claims:

Please add new claims 19-38, as follows:

--19. (New) A process for preparing a crosslinker-free composition, said process comprising:

(a) providing an aqueous mixture of a chitosan, wherein the aqueous mixture has a viscosity of from 1,000 mPas to 100,000 mPas;

(b) combining a precipitant with the aqueous mixture to form a crosslinker-free chitosan composition; and

(c) drying the crosslinker-free chitosan composition to form a crosslinker-free three-dimensional structure.--

--20. (New) The process according to claim 19, wherein the aqueous mixture is present in a state selected from the group consisting of solutions and homogenous suspensions.--

--21. (New) The process according to claim 19, wherein the chitosan is present in an amount of from 0.1 to 15% by weight, based on the aqueous mixture.--

--22. (New) The process according to claim 19, wherein the aqueous mixture has a pH value of from 1 to 7.5.--

--23. (New) The process according to claim 19, wherein the aqueous mixture has a viscosity of from 10,000 mPas to 40,000 mPas.--

--24. (New) The process according to claim 19, wherein the chitosan comprises a cationically-derivatized chitosan.--

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--25. (New) The process according to claim 19, wherein the precipitant comprises an aqueous solution selected from the group consisting of aqueous solutions of hydrogen carbonates, carbonates, hydrogen phosphates, hydroxides of alkali metals, alkaline earth metals, ammonia and organic nitrogen bases, and combinations thereof.--

--26. (New) The process according to claim 19, wherein the precipitant comprises an aqueous solution of sodium hydrogen carbonate.--

--27. (New) The process according to claim 19, wherein the crosslinker-free chitosan composition formed in step (b) has a pH value of from 5 to 14.--

--28. (New) The process according to claim 19, wherein the drying of the crosslinker-free chitosan composition comprises freeze-drying.--

--29. (New) The process according to claim 19, further comprising combining one or more auxiliaries or additives with the aqueous mixture prior to drying.--

--30. (New) The process according to claim 19, further comprising combining one or more auxiliaries or additives with the crosslinker-free composition subsequent to drying.--

--31. (New) A process for preparing a crosslinker-free composition, said process comprising:

(a) providing an aqueous mixture of a cationically-derivatized chitosan, wherein the aqueous mixture has a viscosity of from 10,000 mPas to 40,000 mPas and a pH value of from 1 to 7.5;

(b) combining a precipitant selected from the group consisting of aqueous solutions of hydrogen carbonates, carbonates, hydrogen phosphates, hydroxides of

alkali metals, alkaline earth metals, ammonia and organic nitrogen bases, and combinations thereof, with the aqueous mixture to form a crosslinker-free chitosan composition; and

(c) freeze-drying the crosslinker-free chitosan composition to form a crosslinker-free three-dimensional structure.--

--32. (New) A crosslinker-free, chitosan composition prepared by the process according to claim 19.--

--33. (New) A crosslinker-free, chitosan composition prepared by the process according to claim 23.--

--34. (New) A crosslinker-free, chitosan composition prepared by the process according to claim 25.--

--35. (New) A crosslinker-free, chitosan composition prepared by the process according to claim 28.--

--36. (New) A crosslinker-free, chitosan composition prepared by the process according to claim 31.--

--37. (New) A cosmetic preparation comprising a crosslinker-free, chitosan composition prepared by the process according to claim 19.--

--38. (New) A food additive comprising a crosslinker-free, chitosan composition prepared by the process according to claim 19.--

Please cancel claims 1-18, without prejudice.

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REMARKS

Claims 19-38 are currently pending in the instant application.

The Specification has been amended to delete the original section headings and to insert the preferred section headings pursuant to 37 C.F.R. §1.77. A new Title of the Invention has been inserted. An Abstract of the Disclosure, in accordance with the disclosure, has been added. It is submitted that the amendments to the Specification made herein introduce no new matter. All of the amendments to the Specification constitute deletions of original section headings and/or paragraphs, and insertions or additions of new section headings and/or paragraphs. Accordingly, pursuant to 37 C.F.R. §1.121(b)(1)(iii), no separate page captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE" is necessary. A separate page containing a clean copy of the Abstract of the Disclosure has been attached for the Examiner's convenience. Entry of the amendments to the Specification made herein are therefore proper and respectfully requested.

Original claims 1-18 have been canceled and replaced with new claims 19-38 solely for the purpose of improving clarity and grammar, which may suffer in translation, and not for any reason which relates to the statutory requirements for a patent. New claims 19-38 have not been added in response to any rejection, nor in anticipation of any rejection. Applicants respectfully submit that the scope of new claims 19-38 generally corresponds to the scope of original claims 1-18, and that new claims 19-38 are no narrower than original claims 1-18. Furthermore, although a moot point in view of their cancellation, Applicants respectfully submit that original claims 1-18 satisfied the requirements of 35 U.S.C. §112, as filed. New claims 19-38 are supported by the claims as originally filed and in the Specification, for example, at page 3, lines 4-16; at page 6, lines 11-26; at page 7, lines 1-25; at page 11, lines 4-6; and in the Examples. No new matter has been introduced. All of the amendments to the Claims constitute cancellation of original claims and the addition of new claims. Accordingly, pursuant to 37 C.F.R. §1.121(c)(1)(ii), no separate page captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE" is necessary. Entry is therefore proper and respectfully requested.

Preliminary Amendment of U.S. National Stage for International Application PCT/EP00/06162 filed July 1, 2000

Prompt examination of the instant application in view of the amendments made herein is respectfully requested.

Respectfully submitted,

ANDREA HEILEMANN, *et al.*

January 14, 2002
(Date)

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Preparations Containing No Crosslinking Agents

Field of the Invention

This invention relates generally to biopolymers and more particularly to crosslinker-free preparations obtained by precipitation and subsequent drying of chitosans and to a process for their production.

Prior Art

Beauty packs containing chitosan as their active component and organic acids and collagen as further constituents are known from Japanese patent application **JP-A2 Hei 6/048 917** (Nagawa). Japanese patent application **JP-A2 Hei 4/275 207** (Nitta Gelatin) relates to moisture-binding additives for skin cosmetics in the form of powder-form mixtures of chitosan and collagen. European patent application EP A2 627 225 (Hüls) describes superabsorbents of acid-reacted chitosans which are present in powder form.

German patent application **DE-A1 196 43 066** (Henkel) describes collagen-free cosmetic preparations obtained by crosslinking cationic biopolymers with diisocyanates and/or dialdehydes. US Patent **US 5,322,935** (Allied Signal Inc.) relates to highly porous crosslinked materials of nitrogen-containing polymers and to a process for their production. In this process, a nitrogen-containing polymer is first dissolved in water or an aqueous acid, then ionically crosslinked with an anionic salt solution and, finally, is covalently crosslinked with crosslinking agents. Dialdehydes and aromatic and aliphatic diisocyanates are mentioned as examples of crosslinking agents. International patent application **WO 96/20015** (Kimberly-Clark) describes water-swellable, water-insoluble chitosan salts with a defined absorption capacity under external pressure which can be prepared by crosslinking. Japanese patent application **JP-A2 03165775**

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(Katakura Chikkarin Co.) describes the production of N-succinyl chitosans in the form of a multiporous sponge or film by crosslinking with hexamethylene diisocyanate. These sponges or films are suitable as a prosthetic material for wound dressings, artificial blood vessels or styptic dressings. European patent **EP-B1 663 212** (Hydromer Inc.) describes gels obtained by crosslinking chitosans with polyvinyl pyrrolidone.

One feature common to all the known products is that the biopolymers are linked by chemical crosslinking of reactive centers of the biopolymers. In general, bifunctional reagents, such as dialdehydes or diisocyanates for example, are used for this purpose. Since the complete reaction of these chemical crosslinkers generally cannot be taken for granted, residues of the crosslinkers can remain in the product. This can cause irritations or allergic reactions, particularly in the case of preparations that remain on the skin for prolonged periods, such as cosmetics or healing aids, particularly masks, or wound dressings. This is a serious disadvantage, particularly in the case of wound dressings that are applied to already irritated or damaged skin. In addition, biodegradability is impaired by the addition of these chemical crosslinking agents.

In addition, products crosslinked with the usual chemical crosslinking agents cannot be used as foods or food supplements or as drug carriers for oral applications.

Accordingly, the problem addressed by the present invention was to provide crosslinker-free preparations which would have properties comparable with those of known preparations produced using crosslinking agents. In particular, it would be possible to produce a three-dimensional structure in the form of a block, nonwoven or mask. Particular attention would be directed in this regard to such properties as mechanical stability in both the dry and the wet state, swellability and compatibility with other possible ingredients. In addition, production would be simple and variable according to the required properties of the end product. The products

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would also be biodegradable.

Description of the Invention

The present invention relates to crosslinker-free preparations obtainable by adding precipitants to aqueous solutions and/or homogenized suspensions of chitosans and then drying the chitosans.

It has surprisingly been found that the preparations obtainable in this way have properties comparable with those of known crosslinker-containing preparations. In particular, it is possible with the preparations according to the invention to produce three-dimensional structures, such as blocks, nonwovens or masks, which are comparable with the known products in regard to their mechanical stability, elasticity, swellability, water absorbtion capacity and compatibility with other ingredients. In addition, the preparations according to the invention show high dermatological compatibility and are biodegradable. They are also easy to produce on an industrial scale.

The mechanical stability of the preparations according to the invention, measured as tensile strength at break to **DIN 53 571**, test specimen B, is in the range from 10 to 1,000 mN/mm^2 and preferably in the range from 50 to 200 in the dry state and between 10 and 500 and preferably between 30 and 100 mN/mm^2 in the wet state. Their elasticity, measured as elongation at break in % to DIN 53 571, test specimen B, is between 1 and 50% and more particularly between 5 and 20% in the dry state.

The preparations according to the invention have a water absorption capacity of at least 5 g water/g product and, more particularly, of at least 15 g water/g product. To determine water absorption, the material is moistened with deionized water and weighed.

The present invention also relates to a process for the production of crosslinker-free preparations, characterized in that precipitants are added

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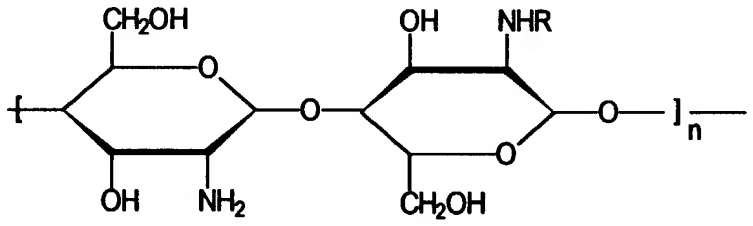
to aqueous solutions and/or homogenized suspensions of chitosans and the chitosans are then dried.

In contrast to chemical crosslinking, the process according to the invention is based on the observation that the addition of the precipitants results in a shift of the pH value which in turn results in partial or complete precipitation and, at the same time, in physical crosslinking of the biopolymer. In contrast to chemical crosslinking, the fibers are not crosslinked by covalent bonds, but presumably through the formation of ion pairs, electrostatic attraction and mechanical entanglement of the fibers.

Accordingly, "crosslinker-free" in the context of the present invention means that the mechanical stability of the preparation is attributable above all to physical crosslinking and, more particularly, that no chemical crosslinking agents, such as bifunctional or multifunctional reagents (for example dialdehydes or diisocyanates), are used for crosslinking.

Chitosans

Chitosans are biopolymers which belong to the group of hydrocolloids. Chemically, they are partly deacetylated chitins differing in their molecular weights which contain the following – idealized – monomer unit:



In contrast to most hydrocolloids, which are negatively charged at biological pH values, chitosans are cationic biopolymers under these conditions. The positively charged chitosans are capable of interacting with oppositely charged surfaces and are therefore used in cosmetic hair-care and body-

care products and pharmaceutical preparations (cf. **Ullmann's Encyclopedia of Industrial Chemistry,** 5th Ed., Vol. A6, Weinheim, Verlag Chemie, 1986, pages 231-332). Overviews of this subject have also been published, for example, by B. Gesslein et al. in **HAPPI** 27, 57 (1990), O. Skaugrud in **Drug Cosm. Ind.** 148, 24 (1991) and E. Onsoyen et al. in **Seifen-Öle-Fette-Wachse** 117, 633 (1991). Chitosans are produced from chitin, preferably from the shell residues of crustaceans which are available in large quantities as inexpensive raw materials. In a process described for the first time by Hackmann et al., the chitin is normally first deproteinized by addition of bases, deminerlized by addition of mineral acids and, finally, deacetylated by addition of strong bases, the molecular weights being distributed over a broad spectrum. Corresponding processes are known, for example, from **Makromol. Chem.** 177, 3589 (1976) or French patent application **FR 2701266 A**. Preferred types are those which are disclosed in German patent applications **DE 4442987 A1** and **DE 19537001 A1** (Henkel) and which have an average molecular weight of 10,000 to 500,000,000 dalton, more particularly 10,000 to 500,000 dalton or 800,000 to 1,200,000 dalton and/or a Brookfield viscosity (1% by weight in glycolic acid) below 30,000 mPas, a degree of deacetylation of 80 to 88% and an ash content of less than 0.3% by weight. Besides chitosans as typical cationic biopolymers, derivatized chitosans where the cationic character is maintained by the derivatization are also suitable for use in accordance with the invention.

Aqueous solutions and/or homogenized suspensions

The chitosans are used as aqueous solutions and/or homogenized suspensions. In general, the chitosans are dissolved or suspended in aqueous mineral acids or aqueous organic carboxylic acids. The suspensions of the chitosans generally contain dissolved fractions of chitosans. Suitable mineral acids are hydrochloric acid, phosphoric acid,

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nitric acid and sulfuric acid. Suitable organic carboxylic acids include formic acid, lactic acid, propionic acid, maleic acid, pyruvic acid, glycolic acid, succinic acid, acetic acid, citric aid, tartaric acid and adipic acid. Hydrochloric acid, lactic acid and glycolic acid are particularly preferred. The acid is used in the quantities required to partly or completely dissolve the chitosan. These are usually 10^{-4} to 10^{-2} mol acid groups per g chitosan and more particularly 1 - 3 x 10^{-3} mol acid groups/g chitosan.

A 0.1 to 15% by weight aqueous solution or suspension is generally used, a 0.5 to 10% by weight and more particularly a 1.0 to 5.0% by weight aqueous solution or suspension being preferred and a 1.5 to 2.5% by weight aqueous solution or suspension being most particularly preferred. It has proved to be of advantage in this regard to adjust the concentration of the aqueous solution and/or suspension to such a value that the solution or suspension has a Brookfield viscosity of 1,000 to 100,000 mPas at 20°C. A viscosity of 10,000 to 40,000 mPas and preferably in the range from 15,000 to 35,000 mPas has proved to be particularly advantageous. In the case of a suspension which generally contains dissolved fractions, it can be of advantage to homogenize the suspension to obtain the required viscosity. In principle, any known methods of homogenization, for example using colloid mills or gap homogenizers, are suitable for this purpose. It has proved to be of particular advantage to use a colloid mill to prepare the homogenized suspensions. Homogenization is generally carried out at temperatures in the range from 0 to 100°C and more particularly at temperatures of 30 to 65°C. The aqueous solution or homogenized suspension generally has a pH of 1.0 to 7.5 and more particularly in the range from 4.5 to 6.5.

Precipitants

In principle, any substances which increase the pH of the aqueous solution or homogenized suspension are suitable as precipitants for the

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purposes of the invention. Aqueous solutions of carbonates, hydrogen carbonates, hydrogen phosphates and hydroxides of the alkali and alkaline earth metals, ammonia and organic nitrogen bases may be used for this purpose. Suitable organic nitrogen bases are, for example, triethylamine, triethanolamine or tetraalkyl ammonium hydroxides. The aqueous solutions of the precipitants are normally used in a concentration of 5 to 20% by weight and more particularly 7 to 16% by weight. In one preferred embodiment of the present invention, an aqueous sodium hydrogen carbonate solution, more particularly a 7 to 16% by weight and preferably a 7 to 9% by weight aqueous sodium hydrogen carbonate solution, is used as the precipitant.

The present invention includes the observation that the mechanical properties of the end product can be influenced through the ratio of precipitant (base) to the quantity of acid present. If complete precipitation of the chitosan is required, the base is used in an equimolar quantity to the acid (generally 0.8 -1.2 mol base:1 mol acid, more particularly 0.9 - 1.1 mol base:1 mol acid and most particularly 1 mol base:1 mol acid). If the requirements which the mechanical properties of the end product are expected to satisfy are less stringent, partial precipitation with less than the equimolar quantity of base can be carried out. Where high alkalinity is required in the end product, a molar excess of base may be used.

Through the treatment with the precipitant, the pH of the aqueous solution or homogenized suspension of the biopolymers is generally adjusted to a value of 5.0 to 14 and more particularly to a value of 7.0 to 8.5.

Drying

The present invention includes the observation that the mechanical stability of the end product can be influenced through the choice of the method used for drying and through the parameters of the particular

method selected.

Suitable drying methods are, for example, air drying, vacuum drying, more particularly at temperatures of 20 to 100°C or above 100°C, and freeze drying.

In one preferred embodiment of the present invention, freeze drying is used for drying.

It has proved to be particularly suitable for drying to be preceded by a freezing step. This is particularly advantageous in combination with freeze drying. The present invention includes the observation that the structure produced by precipitation of the fibers, which is fixed by the freezing step, remains substantially intact where drying is carried out by freeze drying. To this end, the suspension adjusted to the required viscosity and mixed with precipitants is frozen at temperatures below the freezing point taking the desired geometric form into consideration. The way in which the freezing step is carried out has a major bearing on the appearance and structure of the sponge formed after freeze drying. For example, the quicker the freezing step, the more finely porous and uniform the sponge formed after freeze drying will be. The freezing step may be carried out in standard freezing baths or even in refrigerators using liquefied gases, more particularly liquid nitrogen, as the refrigerating medium. Temporary storage of the frozen suspension for up to several days or weeks is possible in principle and does not adversely affect the quality of the end product.

Freeze drying is carried out by known methods as described, for example, by G.W. Oetjen in **Gefriertrocknen, Wiley-VCH Verlag, 1997, 1st Edition, Weinheim**. It has proved to be of advantage to carry out freeze drying in such a way that no part of the frozen material thaws either partly or completely at any time. From the economic perspective, it has proved to be of advantage to accelerate the drying process by applying energy, for example through radiant heat. To avoid discolorations, it is of

advantage to increase temperatures in the already dried parts of the product at most to such a level that no product damage occurs.

Production of the preparations

Normally, aqueous solutions or suspensions of the chitosans with a dry matter content of 0.1 to 15, preferably 0.5 to 10, more preferably 1.0 to 5.0% by weight and most preferably 1.5 to 2.5% by weight are prepared at a pH of 1.0 to 7.5 and preferably 4.5 to 6.5 by addition of inorganic or organic acids, preferably hydrochloric acid, glycolic acid and/or lactic acid, the temperature having to be selected so that it supports swelling of the chitosan. The temperature is normally in the range from 0 to 100°C and preferably in the range from 30 to 65°C. Besides dissolved chitosan, the suspensions prepared in this way also contain swollen undissolved particles. The viscosity of the suspension adjusted through the conditions mentioned can influence the later mechanical properties of the nonwovens.

To improve elasticity in the dried state, polyols and other auxiliaries and additives may then be added to the suspensions. In addition, it has proved to be of advantage so far as the mechanical properties of the preparations are concerned to add natural fibers, for example lignin, polyose, pectin and in particular cellulose, or synthetic fibers, for example polyesters, polyamides, or mixtures thereof to the suspensions in a quantity of 1 to 50% by weight and preferably 5 to 10% by weight. It is particularly advisable to add the fibers to the solution or suspension before homogenization. The suspensions are then homogenized. After their preparation in the desired viscosity range, the aqueous solutions and/or homogenized suspensions are generally degassed, for example by vacuum or ultrasound, to avoid the entrapment of gas bubbles.

The addition and homogeneous distribution of the precipitant can be carried out so quickly (generally 1 to 10 and preferably 1 to 4 minutes) that the precipitation and physical crosslinking of the chitosan mainly takes

place after the corresponding freezing mold has been filled. It has proved to be of particular advantage so far as the development of physical crosslinking is concerned to allow the product to stand for 10 mins. to 10 hours and more particularly for 30 mins. to 6 hours without any further mixing. The precipitant may be added through a mixing element with static and/or moving internals. The resulting suspension can be introduced into a suitable mold corresponding to the geometric shape required for the end product. Depending on the shape required for the end product, the mold may be a bowl, tube, hose, syringe, etc. Different layer thicknesses of the end product can be adjusted in freezing bowls through the filling level of the suspension. Layer thicknesses of 1 to 100 mm and more particularly 15 to 35 mm can be adjusted for the production of preparations in the form of nonwovens which are used, for example, as cosmetic products or healing aids or medicinal products.

A freezing phase is then normally carried out before the preparation is dried.

The addition of other auxiliaries and additives may be carried out both before and together with the addition of the precipitant. The other auxiliaries and additives are preferably added before the precipitant. In this case, too, it is of advantage to adjust the solutions or suspensions containing the other auxiliaries and additives to a viscosity of 1,000 to 100,000, preferably to a viscosity of 10,000 to 40,000 and more preferably to a viscosity of 15,000 to 35,000 mPas before the precipitant is added.

In another embodiment of the invention, the crosslinker-free preparations are charged with auxiliaries and additives after drying. In this case, cosmetic and pharmaceutical active components or flavors, for example, are applied by special techniques to the final dry preparation after freeze drying. To this end, the active component is dissolved in a suitable solvent, applied to the sponge formed after freeze drying, which in this embodiment, acts as a carrier material and the solvent is then carefully

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removed. Suitable solvents are, for example, supercritical CO_2 or nonpolar or polar organic solvents such as, for example, hexane, ethanol or isopropanol.

The present invention includes the observation that, in a crosslinker-free preparation, auxiliaries and additives may be added both before or together with the precipitant and also after drying.

Auxiliaries and additives

The auxiliaries and additives used may be substances which are compatible with the crosslinker-free preparations and which positively influence the physical properties of the preparations and/or impart additional functions to the preparations. Particularly preferred auxiliaries and additives are substances selected from the group consisting of polyols, emulsifiers, fibers, dyes, perfume oils, flavors, cosmetic active components, pharmaceutical active principles and food additives.

The preparations according to the invention may contain small quantities of oil components, synthetic and natural hydrocarbons, waxes, cationic polymers, thickeners, silicone compounds, biogenic agents, film formers, preservatives, solubilizers, structure formers and protective solutions (cryoprotectant agents = CPA), UV protection factors and the like as further auxiliaries and additives.

Polyols suitable for use in accordance with the invention as additional constituents of the crosslinker-free preparations preferably contain 2 to 15 carbon atoms and at least two hydroxyl groups. Typical examples are

- glycerol;
- alkylene glycols such as, for example, ethylene glycol, diethylene glycol, propylene glycol, butylene glycol, hexylene glycol and polyethylene glycols with an average molecular weight of 100 to 1,000 dalton;

- technical oligoglycerol mixtures with a degree of self-condensation of 1.5 to 10 such as, for example, technical diglycerol mixtures with a diglycerol content of 40 to 50% by weight;
- lower alkyl glucosides, particularly those containing 1 to 8 carbon atoms in the alkyl group, for example methyl and butyl glucoside;
- sugar alcohols containing 5 to 12 carbon atoms, for example sorbitol or mannitol,
- sugars containing 5 to 12 carbon atoms, for example glucose or sucrose;
- aminosugars, for example glucamine.

The polyols are normally used in quantities of 0.1 to 20% by weight and preferably in quantities of 1 to 10% by weight, based on the dry matter content of the chitosan. Glycerol and polyethylene glycols are preferably used as the polyols.

Suitable **emulsifiers** are, for example, nonionic surfactants from at least one of the following groups:

(b1) products of the addition of 2 to 30 moles ethylene oxide and/or 0 to 5 moles propylene oxide onto linear fatty alcohols containing 8 to 22 carbon atoms, onto fatty acids containing 12 to 22 carbon atoms and onto alkylphenols containing 8 to 15 carbon atoms in the alkyl group;

(b2) $C_{12/18}$ fatty acid monoesters and diesters of adducts of 1 to 30 moles of ethylene oxide with glycerol;

(b3) glycerol monoesters and diesters and sorbitan monoesters and diesters of saturated and unsaturated fatty acids containing 6 to 22 carbon atoms and ethylene oxide adducts thereof;

(b4) alkyl mono- and oligoglycosides containing 8 to 22 carbon atoms in the alkyl group and ethoxylated analogs thereof;

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(b5) products of the addition of of 15 to 60 moles ethylene oxide onto castor oil and/or hydrogenated castor oil;

(b6) polyol esters and, in particular, polyglycerol esters such as, for example, polyglycerol polyricinoleate or polyglycerol poly-12-hydroxystearate. Mixtures of compounds from several of these classes are also suitable;

(b7) products of the addition of 2 to 15 moles ethylene oxide with castor oil and/or hydrogenated castor oil;

(b8) partial esters based on linear, branched, unsaturated or saturated $C_{12/22}$ fatty acids, ricinoleic acid and 12-hydroxystearic acid and glycerol, polyglycerol, pentaerythritol, dipentaerythritol, sugar alcohols (for example sorbitol) and polyglucosides (for example cellulose);

(b9) trialkyl phosphates;

(b10) wool wax alcohols;

(b11) polysiloxane/polyalkyl polyether copolymers and corresponding derivatives;

(b12) mixed esters of pentaerythritol, fatty acids, citric acid and fatty alcohol according to **DE-PS 11 65 574** and/or mixed esters of fatty acids containing 6 to 22 carbon atoms, methyl glucose and polyols, preferably glycerol, and

(b13) polyalkylene glycols.

The addition products of ethylene oxide and/or propylene oxide onto fatty alcohols, fatty acids, alkylphenols, glycerol monoesters and diesters and sorbitan monoesters and diesters of fatty acids or onto castor oil are known commercially available products. They are homolog mixtures of which the average degree of alkoxylation corresponds to the ratio between the quantities of ethylene oxide and/or propylene oxide and substrate with which the addition reaction is carried out. $C_{12/18}$ fatty acid monoesters and

diesters of addition products of ethylene oxide onto glycerol are known as refatting agents for cosmetic formulations from **DE-PS 20 24 051**.

$C_{8/18}$ alkyl mono- and oligoglycosides, their production and their use as surfactants are known, for example, from **US 3,839,318, US 3,707,535, US 3,547,828, DE-OS 19 43 689, DE-OS 20 36 472** and **DE-A1 30 01 064** and also from **EP-A 0 077 167**. They are produced in particular by reacting glucose or oligosaccharides with primary C_{8-18} alcohols. So far as the glycoside unit is concerned, both monoglycosides in which a cyclic sugar unit is attached to the fatty alcohol by a glycoside bond and oligomeric glycosides with a degree of oligomerization of preferably up to about 8 are suitable. The degree of oligomerization is a statistical mean value on which the homolog distribution typical of such technical products is based.

The emulsifiers are normally used in quantities of 0.1 to 20% by weight and preferably in quantities of 1 to 10% by weight, based on the dry matter content of the chitosan.

Suitable **oil components** are, for example, Guerbet alcohols based on C_{6-18} and preferably C_{8-10} fatty alcohols, esters of linear C_{6-20} fatty acids with linear C_{6-20} fatty alcohols, esters of branched C_{6-13} carboxylic acids with linear C_{6-20} fatty alcohols, esters of linear C_{6-18} fatty acids with branched alcohols, more particularly 2-ethyl hexanol, esters of linear and/or branched fatty acids with polyhydric alcohols (for example dimer diol or trimer triol) and/or Guerbet alcohols, triglycerides based on C_{6-10} fatty acids, esters of C_{6-22} fatty alcohols and/or Guerbet alcohols with aromatic carboxylic acids, more particularly benzoic acid, vegetable oils, branched primary alcohols, substituted cyclohexanes, Guerbet carbonates, dialkyl ethers, silicone oils and/or aliphatic or naphthenic hydrocarbons.

Examples of **synthetic hydrocarbons** which may be used in accordance with the invention are hydrogenated polyisobutene (synthetic squalane), polyisobutene, polyethylene, polypropylene. Suitable **natural hydrocarbons** are terpenes, for example squalene or squalane. The

hydrocarbons are normally used in quantities of 0.1 to 20% by weight and preferably in quantities of 1 to 10% by weight, based on the dry matter content of the chitosans.

Suitable **thickeners** are, for example, polysaccharides, more especially xanthan gum, guar-guar, agar-agar, alginates and tyloses, carboxymethyl cellulose and hydroxyethyl cellulose, also relatively high molecular weight polyethylene glycol monoesters and diesters of fatty acids, polyacrylates, polyvinyl alcohol and polyvinyl pyrrolidone.

Suitable **cationic polymers** are, for example, cationic cellulose derivatives, cationic starch, copolymers of diallyl ammonium salts and acrylamides, quaternized vinyl pyrrolidone/vinyl imidazole polymers such as, for example, Luviquat® (BASF AG, Ludwigshafen, FRG), condensation products of polyglycols and amines, quaternized collagen polypeptides such as, for example, Lauryldimonium Hydroxypropyl Hydrolyzed Collagen (Lamequat®L, Grünau GmbH), quaternized wheat polypeptides, polyethyleneimine, cationic silicone polymers such as, for example, amodimethicone or Dow Corning, Dow Corning Co., USA, copolymers of adipic acid and dimethylaminohydroxypropyl diethylenetriamine (Cartaretine®, Sandoz AG, CH), polyaminopolyamides as described, for example, in **FR-A 2 252 840** and crosslinked water-soluble polymers thereof, cationic chitin derivatives such as, for example, quaternized chitosan, optionally in microcrystalline distribution, condensation products of dihaloalkyls, for example dibromobutane, with bis-dialkylamines, for example bis-dimethylamino-1,3-propane, cationic guar gum such as, for example, Jaguar® CBS, Jaguar® C-17, Jaguar® C-16 of Celanese, USA, quaternized ammonium salt polymers such as, for example, Mirapol® A-15, Mirapol® AD-1, Mirapol® AZ-1 of Miranol, USA.

Suitable **silicone compounds** are, for example, dimethyl polysiloxanes, methylphenyl polysiloxanes, cyclic silicones and amino-, fatty acid-, alcohol-, polyether-, epoxy-, fluorine- and/or alkyl-modified silicone com-

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pounds which may be both liquid and resin-like at room temperature.

In the context of the invention, **biogenic agents** are, for example, bisabolol, allantoin, phytantriol, panthenol, AHA acids, plant extracts, marine extracts, vitamins and vitamin complexes.

Film formers are, for example, chitosan, microcrystalline chitosan, quaternized chitosan, polyvinyl pyrrolidone, vinyl pyrrolidone/vinyl acetate copolymers, polymers of the acrylic acid series, quaternary cellulose derivatives, collagen, hyaluronic acid and salts thereof and similar compounds.

The **dyes** used may be selected from any of the substances which are approved and suitable for cosmetic purposes, as listed for example in the publication **"Kosmetische Färbemittel"** of the Farbstoffkommission der Deutschen Forschungsgemeinschaft, published by Verlag Chemie, Weinheim, 1984, pages 81-106. These dyes are typically used in concentrations of 0.001 to 0.1% by weight, based on the mixture as a whole.

The **fibers** used may be both natural fibers and synthetic fibers and mixtures thereof. Suitable natural fibers are, for example, lignin, polyose, pectin and, in particular, cellulose. Suitable synthetic fibers are, for example, polyesters, polyamides or mixtures thereof. The fibers are preferably used in a quantity of 1 to 50% by weight and preferably in a quantity of 5 to 10% by weight.

Waxes are natural or synthetic substances which are are kneadable at 20°C, solid to fragile and hard, coarsely to finely crystalline, transparent to opaque, but not glass-like, melt without decomposing above 40°C and are of comparatively low viscosity and non-stringing even just above their melting point. The waxes suitable for use in accordance with the invention differ from resins, for example, in the fact that they change into a molten low-viscosity state at temperatures of generally about 50 to 90°C, in exceptional cases even as high as 200°C, and are substantially free from ash-forming compounds. The waxes are divided into the following three

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groups according to their origin: **natural waxes** such as, for example, candelilla wax, carnauba wax, Japan wax, espartograss wax, cork wax, guaruma wax, rice oil wax, sugar cane wax, ouricury wax, montan wax, beeswax, shellac wax, spermaceti, lanolin (wool wax), uropygial fat, ceresine, ozocerite (earth wax), petrolatum, paraffin waxes and microwaxes; **chemically modified waxes** (hard waxes) such as, for example, montan ester waxes, sasol waxes, hydrogenated jojoba waxes and **synthetic waxes** such as, for example, polyalkylene waxes and polyethylene glycol waxes. In this connection, natural waxes, especially vegetable waxes, are preferred.

Flavors are concentrated preparations of aromas or flavoring agents which are intended to give foods a particular aroma or taste. Examples are vanillin, peppermint oil, Maillard products, banana flavoring and many others. Important aroma carriers are the essential oils and mixtures of individual, generally synthetically produced, so-called "nature-identical" components of these oils. At present, there are about 600 natural and about 4,200 nature-identical aromas for foods, cosmetic products and pharmaceutical products. Suitable **perfume oils** are, for example, mixtures of natural and synthetic perfumes. Natural perfumes include the extracts of blossoms, stems and leaves, fruits, fruit peel, roots, woods, herbs and grasses, needles and branches, resins and balsams. Animal raw materials, for example civet and beaver, may also be used. Typical synthetic perfume compounds are products of the ester, ether, aldehyde, ketone, alcohol and hydrocarbon type. Examples of perfume compounds of the ester type are benzyl acetate, p-tert.butyl cyclohexylacetate, linalyl acetate, phenyl ethyl acetate, linalyl benzoate, benzyl formate, allyl cyclohexyl propionate, styrallyl propionate and benzyl salicylate. Ethers include, for example, benzyl ethyl ether while aldehydes include, for example, the linear alkanals containing 8 to 18 carbon atoms, citral, citronellal, citronellyloxyacetaldehyde, cyclamen aldehyde, hydroxy-

citronellal, lilial and bourgeonal. Examples of suitable ketones are the ionones and methyl cedryl ketone. Suitable alcohols are anethol, citronellol, eugenol, isoeugenol, geraniol, linalool, phenylethyl alcohol and terpineol. The hydrocarbons mainly include the terpenes and balsams. However, it is preferred to use mixtures of different perfume compounds which, together, produce an agreeable fragrance. Other suitable perfume oils are essential oils of relatively low volatility which are mostly used as aroma components. Examples are sage oil, camomile oil, clove oil, melissa oil, mint oil, cinnamon leaf oil, lime-blossom oil, juniper berry oil, vetiver oil, olibanum oil, galbanum oil, labolanum oil and lavendin oil. The following are preferably used either individually or in the form of mixtures: bergamot oil, dihydromyrcenol, lilial, lyral, citronellol, phenylethyl alcohol, α-hexylcinnamaldehyde, geraniol, benzyl acetone, cyclamen aldehyde, linalool, Boisambrene Forte, Ambroxan, indole, hedione, sandelice, citrus oil, mandarin oil, orange oil, allylamyl glycolate, cyclovertal, lavendin oil, clary oil, β-damascone, geranium oil bourbon, cyclohexyl salicylate, Vertofix Coeur, Iso-E-Super, Fixolide NP, evernyl, iraldein gamma, phenylacetic acid, geranyl acetate, benzyl acetate, rose oxide, romilat, irotyl and floramat.

The **food additives** used are substances without or with nutritional value which generally are neither consumed as foods themselves or used as characteristic food additives or added to a food for technological reasons during production, processing, preparation, treatment, packaging, handling or storage so that they themselves or their secondary products become or could become parts of the food. Some food additives are of natural origin such as, for example, carotene from carrots, chlorophyll from green plants, lecithin from eggs or soya beans. Others, by contrast, are purely synthetic chemicals such as, for example, the azo dyes tartrazine and amaranth, the antioxidants BHA and BHT and the sweeteners saccharin and cyclamate.

Pharmaceutical active principles in the context of the invention are active components and healing aids and their vehicles made up in various medicinal forms. Azelaic acid as an antiacne agent and PVP/iodine complex as a disinfectant are mentioned by way of example.

Suitable **cosmetic active components** are any substances which are suitable for use in cosmetic preparations.

Suitable **preservatives** are, for example, phenoxyethanol, formaldehyde solution, parabens, pentanediol or sorbic acid and the other classes of compounds listed in Appendix 6, Parts A and B of the Kosmetikverordnung ("Cosmetics Directive").

Examples of **UV protection factors are** organic substances (light filters) which are liquid or crystalline at room temperature and which are capable of absorbing ultraviolet radiation and of releasing the energy absorbed in the form of longer-wave radiation, for example heat. UV-B filters can be oil-soluble or water-soluble. The following are examples of oil-soluble substances:

- 3-benzylidene camphor or 3-benzylidene norcamphor and derivatives thereof, for example 3-(4-methylbenzylidene)-camphor, as described in **EP 0693471 B1**;
- 4-aminobenzoic acid derivatives, preferably 4-(dimethylamino)-benzoic acid-2-ethylhexyl ester, 4-(dimethylamino)-benzoic acid-2-octyl ester and 4-(dimethylamino)-benzoic acid amyl ester;
- esters of cinnamic acid, preferably 4-methoxycinnamic acid-2-ethylhexyl ester, 4-methoxycinnamic acid propyl ester, 4-methoxycinnamic acid isoamyl ester, 2-cyano-3,3-phenylcinnamic acid-2-ethylhexyl ester (Octocrylene);
- esters of salicylic acid, preferably salicylic acid-2-ethylhexyl ester, salicylic acid-4-isopropylbenzyl ester, salicylic acid homomenthyl ester;
- derivatives of benzophenone, preferably 2-hydroxy-4-methoxybenzo-

phenone, 2-hydroxy-4-methoxy-4'-methylbenzophenone, 2,2'-dihydroxy-4-methoxybenzophenone;

- esters of benzalmalonic acid, preferably 4-methoxybenzalmalonic acid di-2-ethylhexyl ester;
- triazine derivatives such as, for example, 2,4,6-trianilino-(p-carbo-2'-ethyl-1'-hexyloxy)-1,3,5-triazine and Octyl Triazone, as described in **EP 0 818 450 A1**, or Dioctyl Butamido Triazine (Uvasorb® HEB);
- propane-1,3-diones such as, for example, 1-(4-tert.butylphenyl)-3-(4'-methoxyphenyl)-propane-1,3-dione;
- ketotricyclo(5.2.1)decane derivatives, as described in **EP 0 694 521 B1**.

Suitable water-soluble substances are

- 2-phenylbenzimidazole-5-sulfonic acid and alkali metal, alkaline earth metal, ammonium, alkylammonium, alkanolammonium and glucammonium salts thereof;
- sulfonic acid derivatives of benzophenones, preferably 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid and salts thereof;
- sulfonic acid derivatives of 3-benzylidene camphor such as, for example, 4-(2-oxo-3-bornylidenemethyl)-benzene sulfonic acid and 2-methyl-5-(2-oxo-3-bornylidene)-sulfonic acid and salts thereof.

Typical UV-A filters are, in particular, derivatives of benzoyl methane such as, for example 1-(4'-tert.butylphenyl)-3-(4'-methoxyphenyl)-propane-1,3-dione, 4-tert-butyl-4'-methoxydibenzoylmethane (Parsol 1789), 1-phenyl-3-(4'-isopropylphenyl)-propane-1,3-dione and the eneamine compounds described in **DE 19712033 A1** (BASF). The UV-A and UV-B filters may of course also be used in the form of mixtures. Besides the soluble substances mentioned, insoluble pigments, i.e. finely dispersed metal oxides or salts, may also be used for this purpose. Examples of

suitable metal oxides are, in particular, zinc oxide and titanium dioxide and also oxides of iron, zirconium, silicon, manganese, aluminium and cerium and mixtures thereof. Silicates (talcum), barium sulfate and zinc stearate may be used as salts. The oxides and salts are used in the form of the pigments for skin-care and skin-protecting emulsions and decorative cosmetics. The particles should have an average diameter of less than 100 nm, preferably from 5 to 50 nm and more preferably from 15 to 30 nm. They may be spherical in shape although ellipsoidal particles or other non-spherical particles may also be used. The pigments may also be surface-treated, i.e. hydrophilicized or hydrophobicized. Typical examples are coated titanium dioxides such as, for example, Titandioxid T 805 (Degussa) or Eusolex® T2000 (Merck). Suitable hydrophobic coating materials are, above all, silicones and particularly trialkoxyoctyl silanes or simethicones. So-called micro- or nanopigments are preferably used in sun protection products. Micronized zinc oxide is preferably used. Other suitable UV filters can be found in P. Finkel's review in **SÖFW-Journal 122, 543 (1996)**.

Besides the two above-mentioned groups of primary protection factors, secondary protection factors of the **antioxidant** type may also be used. Secondary sun protection factors of the antioxidant type interrupt the photochemical reaction chain which is initiated when UV rays penetrate into the skin. Typical examples of suitable antioxidants are amino acids (for example glycine, histidine, tyrosine, tryptophane) and derivatives thereof, imidazoles (for example urocanic acid) and derivatives thereof, peptides, such as D,L-carnosine, D-carnosine, L-carnosine and derivatives thereof (for example anserine), carotinoids, carotenes (for example α-carotene, β-carotene, lycopene) and derivatives thereof, chlorogenic acid and derivatives thereof, liponic acid and derivatives thereof (for example dihydroliponic acid), aurothioglucose, propylthiouracil and other thiols (for example thioredoxine, glutathione, cysteine, cystine, cystamine and

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glycosyl, N-acetyl, methyl, ethyl, propyl, amyl, butyl and lauryl, palmitoyl, oleyl, γ-linoleyl, cholesteryl and glyceryl esters thereof) and their salts, dilaurylthiodipropionate, distearylthiodipropionate, thiodipropionic acid and derivatives thereof (esters, ethers, peptides, lipids, nucleotides, nucleosides and salts) and sulfoximine compounds (for example butionine sulfoximines, homocysteine sulfoximine, butionine sulfones, penta-, hexa- and hepta-thionine sulfoximine) in very small compatible dosages (for example pmole to μmole/kg), also (metal) chelators (for example α-hydroxyfatty acids, palmitic acid, phytic acid, lactoferrine), α-hydroxy acids (for example citric acid, lactic acid, malic acid), humic acid, bile acid, bile extracts, bilirubin, biliverdin, EDTA, EGTA and derivatives thereof, unsaturated fatty acids and derivatives thereof (for example γ-linolenic acid, linoleic acid, oleic acid), folic acid and derivatives thereof, ubiquinone and ubiquinol and derivatives thereof, vitamin C and derivatives thereof (for example ascorbyl palmitate, Mg ascorbyl phosphate, ascorbyl acetate), liponic acid, tocopherols and derivatives (for example vitamin E acetate), vitamin A and derivatives (vitamin A palmitate) and coniferyl benzoate of benzoin resin, rutinic acid and derivatives thereof, α-glycosyl rutin, ferulic acid, furfurylidene glucitol, carnosine, butyl hydroxytoluene, butyl hydroxyanisole, nordihydroguaiac resin acid, nordihydroguaiaretic acid, trihydroxybutyrophenone, uric acid and derivatives thereof, mannose and derivatives thereof, Superoxid-Dismutase, zinc and derivatives thereof (for example ZnO, $ZnSO_4$), selenium and derivatives thereof (for example selenium methionine), stilbenes and derivatives thereof (for example stilbene oxide, trans-stilbene oxide) and derivatives of these active principles suitable for the purposes of the invention (salts, esters, ethers, sugars, nucleotides, nucleosides, peptides and lipids).

Cryoprotectant agents are, for example, sugar solutions, such as sucrose, maltose or the like, glycerol, PVP or even buffer solutions.

The total percentage content of auxiliaries and additives can be from

0.1 to 50% by weight and is preferably from 0.5 to 10% by weight, based on the dry matter of the chitosan.

Commercial Applications

The preparations according to the invention are distinguished by high dermatological compatibility and a high absorption capacity for liquids. Accordingly, the present invention also relates to the use of the preparations according to the invention as cosmetic preparations, more particularly as dry films, absorbers and cosmetic masks and styptic sponges for small cuts, for example caused by shaving.

The present invention also relates to the use of the preparations according to the invention as healing aids and/or medicinal products, more particularly as wound tampons, wound dressings, burn dressings, bandages releasing active principles, nonwovens and as drug carriers for oral applications. In this embodiment, the preparations according to the invention may be charged with various topical pharmaceutical formulations. For oral applications, the preparations according to the invention may be used, for example, as carriers, for example for antibiotics, analgesics and the like.

The present invention also relates to the use of the preparations according to the invention as foods. Foods in the context of this embodiment are any substances which are intended for human consumption in unmodified, prepared or processed form. Foods under this definition also include in particular food supplements and dietetic foods. In addition, the preparations according to the invention are suitable for use as food additives.

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Examples

Example 1

A suspension of 2 kg chitosan (Hydagen® CMFP, Henkel KGaA), 98 kg water and 0.346 kg L-(+) lactic acid was homogenized in a colloid mill at a temperature of 40°C until a viscosity of 23,000 mPas was reached. The suspension was then cooled to 10°C and degassed in vacuo. 9 kg of the suspension were mixed for 2 minutes with 360 g of an aqueous solution of sodium hydrogen carbonate (= 8.05% by weight aqueous sodium hydrogen carbonate solution) and then poured into molds. The layer thickness of the suspension in the mold was 22 mm. After standing for 3 h, the suspension was frozen and the frozen plates were freeze-dried at 80°C/1 mbar.

The dried blocks were then cut to the required size and thickness (thickness: 1.2 mm, size: 20 x 30 cm).

Example 2

A suspension of 2 kg chitosan, 98 kg water, 0.292 kg glycolic acid, 0.1 kg cellulose fibers and 0.08 kg emulsifier PEG-30 Glyceryl Stearate (Tagat S®, Tego Cosmetics, Goldschmidt) was homogenized in a colloid mill at a temperature of 50°C until a viscosity of 26,000 mPas was reached. The suspension was then cooled to 10°C and degassed in vacuo. 9 kg of the suspension were mixed for 1 minute with 360 g of an aqueous solution of sodium hydrogen carbonate (= 8.05% by weight aqueous sodium hydrogen carbonate solution) and then poured into molds. After standing for 30 mins., the suspension was frozen and the frozen plates were freeze-dried at 80°C/1 mbar.

The dried blocks were then cut to the required size and thickness (thickness: 1.5 mm, size: 20 x 30 cm).

Example 3

A suspension of 2 kg chitosan, 98 kg water, 0.7 kg hydrochloric acid (20% by weight), 0.1 kg cellulose fibers, 0.1 kg glycerol and 0.08 kg emulsifier PEG-30 Glyceryl Stearate (Tagat S®, Tego Cosmetics, Goldschmidt) was homogenized in a colloid mill at a temperature of 60°C until a viscosity of 30,000 mPas was reached. The suspension was then cooled to 10°C and degassed in vacuo. 9 kg of the suspension were mixed for 4 minutes with 360 g of a saturated aqueous solution of sodium hydrogen carbonate and then poured into molds. After standing for 6 h, the suspension was frozen and then freeze-dried at 80°C/1 mbar.

The dried blocks were then cut to the required size and thickness (thickness: 5 mm, size: 5 x 8 cm).

Viscosity measurement

All the viscosities shown were measured with a Brookfield DV1 viscosimeter (spindle 4, speed 12 r.p.m., 20°C).

Mechanical stability, water absorption capacity and wetting time

The mechanical stability of the products obtained in accordance with Examples 1 to 3, measured as tensile strength at break to DIN 53 571, test specimen B, was between 100 and 150 mN/mm^2 in the dry state and between 50 and 70 mN/mm^2 in the wet state. Their elasticity, measured as elongation at break in %, was between 8 and 10% in the dry state.

The preparations according to the invention have a water absorption capacity of ca. 20 g water/g product. To determine water absorption, the material is moistened with deionized water and weighed.

The preparations according to the invention have a wetting time of ca. 1-2 mins. Wettability is determined by the following method: a 26 mm wide and 1.2 mm thick strip of the sample to be measured is taken, immersed at one end in a water-filled tray and then stretched onto a horizontal bench. The wetting time shown is the time which the horizontal

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strip takes to be completely wetted by the capillary forces of the sample alone over a distance of 30 mm.

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CLAIMS

1. Crosslinker-free preparations obtainable by adding precipitants to aqueous solutions and/or homogenized suspensions of chitosans and then drying the chitosans.

2. A process for the production of crosslinker-free preparations, characterized in that precipitants are added to aqueous solutions and/or homogenized suspensions of chitosans and the chitosans are then dried.

3. A process as claimed in claim 2, characterized in that drying is carried out by freeze drying.

4. A process as claimed in claim 2 and/or 3, characterized in that 0.1 to 15% by weight aqueous solutions and/or homogenized suspensions of chitosans are used.

5. A process as claimed in at least one of claims 2 to 4, characterized in that the aqueous solutions and/or homogenized suspensions of chitosans have a pH value of 1 to 7.5.

6. A process as claimed in at least one of claims 2 to 5, characterized in that the viscosity of the aqueous solutions and/or homogenized suspensions of chitosans is in the range from 1,000 to 100,000 mPas.

7. A process as claimed in claim 6, characterized in that the viscosity of the aqueous solutions and/or homogenized suspensions of chitosans is in the range from 10,000 to 40,000 mPas.

8. A process as claimed in at least one of claims 2 to 7, characterized in that cationically derivatized chitosans are used as the chitosans.

9. A process as claimed in at least one of claims 2 to 8, characterized in that the precipitants used are selected from the group consisting of aqueous solutions of hydrogen carbonates, carbonates, hydrogen phosphates and hydroxides of the alkali and alkaline earth metals, ammonia and organic nitrogen bases.

10. A process as claimed in claim 9, characterized in that an aqueous sodium hydrogen carbonate solution is used as the precipitant.

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11. A process as claimed in at least one of claims 2 to 10, characterized in that the pH of the precipitated chitosans is between 5.0 and 14.

12. A process as claimed in at least one of the preceding claims, characterized in that auxiliaries and additives are added to the aqueous solutions and/or homogenized suspensions before or at the same time as the precipitant.

13. A process as claimed in at least one of the preceding claims, characterized in that the crosslinker-free preparations are charged with auxiliaries and additives after drying.

14. A process as claimed in claims 12 and/or 13, characterized in that the auxiliaries and additives used are substances selected from the group consisting of polyols, emulsifiers, fibers, dyes, perfume oils, flavors, cosmetic active components, pharmaceutical active principles and food additives.

15. The use of the crosslinker-free preparations claimed in claim 1 as cosmetic preparations.

16. The use of the crosslinker-free preparations claimed in claim 1 as healing aids and/or medicinal products.

17. The use of the crosslinker-free preparations claimed in claim 1 as foods.

18. The use of the crosslinker-free preparations claimed in claim 1 as food additives.

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JC13 Rec'd PCT/PTO 14 JAN 2002

ABSTRACT OF THE DISCLOSURE

Processes for preparing crosslinker-free, chitosan-containing compositions, comprising: (a) providing an aqueous mixture of a chitosan, wherein the aqueous mixture has a viscosity of from 1,000 mPas to 100,000 mPas; (b) combining a precipitant with the aqueous mixture to form a crosslinker-free chitosan composition; and (c) drying the crosslinker-free chitosan composition to form a crosslinker-free three-dimensional structure; are described. Also described are three-dimensional structures prepared thereby and uses therefor in cosmetics, food additives and medical products.

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DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

☐ Declaration Submitted with Initial Filing OR ☒ Declaration Submitted after Initial Filing

Attorney Docket Number	H 4172 PCT/US
First Named Inventor	HEILEMANN, Andrea
COMPLETE IF KNOWN	
Application Number	10/030,974
Filing Date	05/13/2002
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:
My residence, post office address, and citizenship are as stated below next to my name.
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

PREPARATIONS CONTAINING NO CROSS-LINKING AGENTS

(Title of the Invention)

the specification of which

☐ is attached hereto

OR

☒ was filed on (MM/DD/YYYY) 07/01/2000 as United States Application Number or PCT International Application Number PCT/EP00/06162 and was amended on (MM/DD/YYYY) _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY	Priority Not Claimed	Certified Copy Attached? YES	Certified Copy Attached? NO
199 32 075.6	DE	07/12/1999	☐	☐	☒

☐ Additional foreign application numbers are listed on a supplemental priority sheet attached hereto:

I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	
		☐ Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

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DECLARATION

Page 2

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of Title 35, United States Code §112.1 acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number *(if applicable)*
	PCT/EP00/06162	07/01/2000	

[ ] Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto.

As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

[ ] Firm Name ______ Customer Number or label ______

OR

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: [ ] A petition has been filed for this unsigned

1-00

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Applicant Authority

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[X] Additional inventors are being named on supplemental sheet(s) attached hereto

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DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet

2-00

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3-00

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4-00

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DEX

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

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Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
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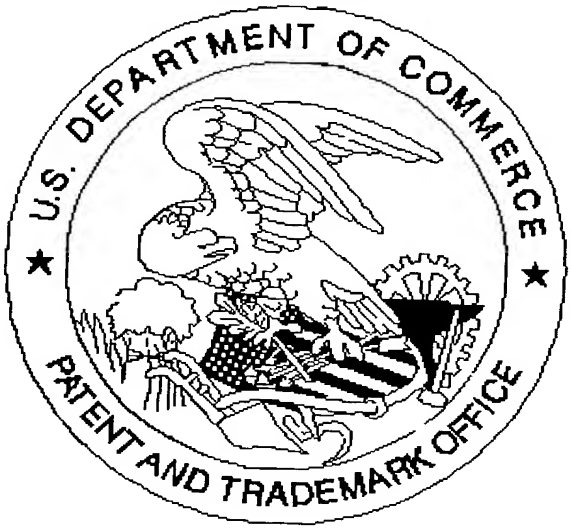

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